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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,726	12/04/2000	Kevin R Stone	56290-054	2424

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/647,726	Stone et al.
Examiner	**Art Unit**
Vera Afremova	1651

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 9, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-48* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-48 are pending and under examination.

Claim Rejections - 35 USC § 112

Claims 14, 25 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 25 and 36 are confusing with regard to concentration of sialic acid as presently claimed which is indicated as being " .01 mM", for example. Is the number intended as being 0.01 mM or 0.1 mM ?

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19, 21-40, 42-51 and 53-59 of U.S. Patent No. 6,231,608 [A] in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts and the xenograft products which are intended for human transplantation wherein the xenograft products comprise "bone tissue", "bone" (6,231,608 [A]) or "a portion of bone tissue" (instant invention) of non-human animal and wherein the xenografts are treated with glucosidase and capping molecules as claimed.

Some of the claims of US 6,231,608 are broader and encompass xenografts such as ligament and articular cartilage which comprise bones or portion of bones (see claims 21-25 42-46 and 53-57) as required for the presently claimed invention. The xenograft products of US 6,231,608 which are comprising bone portions are treated with glycosidase and capping molecules as required by the presently claimed invention.

Some of the claims of US 6,231,608 [A] are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 6,231,608 [A] and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see claims 2 or 24 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods and products are obvious variants. Thus, the inventions as claimed are co-extensive.

2. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-37 of U.S. Patent No. 6,210,440 [B].

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts and the xenograft products intended for human transplantation wherein the xenograft products comprise

"bone" or "a portion of bone tissue" of non-human animal and wherein the xenograft products are treated with glycosidase and capping molecules including sialic acid molecules as claimed.

The claims of US 6,210, 440 [B] are broader and encompass xenograft products such as ligaments which comprise bones or portion of bones (see claims 6, 7, 15, 16, 23, 24, 32, 33, 36 and 37) as required by the presently claimed invention. The whole xenograft products are treated with glycosidase and sialic acid molecules as claimed in US 6,210, 440 [B] and as required by presently claimed invention of the instant application.

The claims of US 6,210, 440 [B] are broader and include the presently claimed concentration ranges of sialic acid, for example: see claim 1 of US 6,210,440 [B] and see instant claim 3. Some of the claims of the instant application appear to be drawn to the use of concentration ranges of sialic acid which are identical to the sialic acid concentration in US 6,210, 440 [B], for example: see claim 1 of US 6,210,440 [B] and the instant claim 14.

Accordingly, the claimed methods and products are obvious variants. Thus, the inventions as claimed are co-extensive.

3. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,402,783 [C] or over claims 1-22 of U.S. Patent No. 5,944,755 [IDS-A33] in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of the patents encompass substantially

similar methods of making xenografts and the xenograft products intended for human transplantation wherein the xenograft products comprise "bone" or "a portion of bone tissue" of non-human animal and wherein the xenograft products are treated with glycosidase and capping molecules as claimed.

Some of the claims of US 6,402,783 [C] or 5,944,755 [IDS-A33] are broader and encompass xenografts such as ligament or articular cartilage, respectively, which comprise bones or portion of bones as required for the presently claimed invention. For example: see US 6,402,783 claims 9, 10, 20, 21, 27 and 28 or see US 5,944,755 claims 8, 17 and 22. The xenografts of both US patents US 6,402,783 [C] and US 5,944,755 [IDS-A33] comprise bone portions which are treated with glycosidase and capping molecules as required by the presently claimed invention.

Some of the claims of US patents US 6,402,783 [C] or 5,944,755 [IDS-A33] are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US patents US 6,402,783 [C] or 5,944,755 [IDS-A33] and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see

specification page 13, line 7) and it encompasses the use of other molecules such as fucosyl and glucosamine in xenografts intended for human transplantation, for example: see instant claims 2 or 24 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods and products are obvious variants. Thus, the inventions as claimed are co-extensive.

4. Claims 23-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,922,027 [IDS-A32].

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar xenograft products intended for human transplantation wherein the xenografts comprise "bone" or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glucosidase as claimed.

Claims of US 5,922,027 [IDS-A32] are broader and encompass xenografts such as articular cartilage comprising bones or portion of bones which are required for the presently claimed invention, for example: see US' 027 claims 2, 4, 6, 7, 13, 15, and 17. The xenograft products of US 5,922,027 [IDS-A32] and of the presently claimed invention which both comprise bones or bone portions are treated with glycosidase as claimed.

Accordingly, the claimed products are obvious variants. Thus, the inventions as claimed are co-extensive.

5. Claims 1-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,782,915 [IDS-A28].

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenograft products intended for human transplantation wherein the xenografts comprise "bone" or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glucosidase as claimed.

Claims of 5,782,915 [IDS-A28] are broader and encompass methods of making xenografts from articular cartilage comprising bones or portion of bones which are required for the presently claimed invention, for example: see US'915 claim 2. US 5,782,915 [IDS-A28] and the presently claimed invention are both drawn to xenografts which are comprising bones or bone portions and which are treated with glycosidase as claimed.

Accordingly, the claimed products are obvious variants. Thus, the inventions as claimed are co-extensive.

6. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,110,206 [IDS-A37].

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts and xenograft products intended for human transplantation wherein the xenografts comprise "bone"

or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glucosidase as claimed.

Claims of 6,110,206 [IDS-A37] are broader and encompass xenografts such as ligament comprising bones or portion of bones which are required for the presently claimed invention, for example: see US'206 claims 6, 7, 14, 15, 18 and 19. The xenografts of US 6,110,206 [IDS-A37] and the xenografts of the presently claimed invention which comprise bones or bone portions are both treated with glycosidase as claimed.

The claims of 6,110,206 [IDS-A37] are broader, they are not limited to the use of capping molecules and they are open to incorporation of additional steps or materials. On the other hand, some of the instant claims do not require the use of capping molecules, for example: see claims 1 and 23. In addition, the use of some generic capping molecules are intended for the xenografts of US 6,110,206 [IDS-A37], for example: see col. 8, lines 13-16.

Accordingly, the claimed products are obvious variants. Thus, the inventions as claimed are co-extensive.

7. Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 6,049,025 [IDS-A36].

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts and xenograft products intended for human transplantation wherein the xenografts comprise "bone"

or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glucosidase and capping molecules including sialic acid molecules as claimed.

The claims of 6,049,025 [IDS-A36] are broader and encompass xenografts such as ligaments which comprise bones or portion of bones (see claims 8, 16, 25, 33 and 36) as required for the presently claimed invention. And the whole xenograft products are treated with glycosidase and sialic acid molecules as claimed in both US 6,049,025 [IDS-A36] and in the instant invention.

Some claims of US 6,049,025 [IDS-A36] are drawn to the use of concentration ranges of sialic acid which are identical to the presently claimed invention, for example: see claims 2, 11, 22 and 28 of US 6,049,025 and see the instant claims 14, 25 and 36. Or the claims of US 6,049,025 [IDS-A36] are broader and include the presently claimed concentration range, for example: see the instant claim 3.

Accordingly, the claimed methods and products are obvious variants. Thus, the inventions as claimed are co-extensive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

> to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-48 are rejected under 35 U.S.C. 103(a) as being obvious over US 6,110,206 [IDS-A37], US 5,944,755 [IDS-A33], US 5,782,915 [IDS-A28] and US 5,922,027 [IDS-A32] taken with Merck Index.

Claims are directed to methods of making xenografts and xenograft products intended for human transplantation wherein the xenografts comprise "bone" or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glycosidase and capping molecules. Some claims are /are further drawn to the use of capping molecules such as sialic acid molecules. Some claims are further drawn to the use of particular concentrations of sialic acid for treatment of xenografts. Some claims are further drawn to the use of glycosidase such as galactosidase, to the use of particular concentration of glycosidase, to the freeze/thaw cycles or gamma irradiation for cellular disruption, to the use of cross linking agents in the methods for making xenografts and xenograft products.

The applied references US 6,110,206 [IDS-A37], US 5,944,755 [IDS-A33], US 5,782,915 [IDS-A28] and US 5,922,027 [IDS-A32] are relied upon as explained above and they teach the similar concepts of making xenografts and xenograft products intended for human transplantation wherein the xenografts comprise "bone" or "a portion of bone tissue" of non-human animal and wherein the xenografts are treated with glycosidase and capping molecules.

For example: US 6,110,206 [A37] discloses ligament xenograft with the bone attached (see col. 5, lines 11-17) which is treated with glycosidase or alpha-galactosidase and with capping molecules (see examples 1 and 2).

US 5,944,755 [IDS-A33] discloses articular cartilage xenograft comprising subchondral bone (see col. 5, lines 60-63) which is treated with glycosidase or alpha-galactosidase and with capping molecules (see examples 1 and 2).

US 5,782,915 [IDS-A28] teaches preparation of articular cartilage xenograft comprising subchondral bone (see col. 4, lines 21-22) which is treated with glycosidase (col. 6, line 34) and with capping molecules (col. 5, line 28).

US 5,922,027 [IDS-A32] teaches an articular cartilage xenograft comprising subchondral bone (see col. 4, lines 23-26) which is free from moieties susceptible to glycosidase digestion (col. 7, line 12) and which is treated with capping molecules (col. 5, line 32).

The cited patents further teach the use of freeze/thaw cycles or gamma irradiation for cellular disruption, the use of cross linking agents in the methods for making xenografts and in the xenograft products. For example: see US 6,110,206 [IDS-A37] at col. 5, lines 36, 46 and 62. See US 5,944,755 [IDS-A33] at col. 6, lines 17, 28 and 44. See US 5,782,915 [IDS-A28] at col. 4, lines 57 and 67. See US 5,922,027 [IDS-A32] at col. 4, line 53 and col. 5, line 2.

The cited patents teach the use of various capping molecules for treating xenograft products including capping molecules such as glucosamines, for example: see US 6,110,206

[IDS-A37] at col. 8, lines 15-16; or see US 5,944,755 [IDS-A33] at col. 9, lines 9-11. But the cited patents are silent with regard to the use of sialic acid.

However, the Merck Index teaches that the capping molecules such as glucosamine and sialic acid are well known compounds which are widely distributed in animal mucoproteins and mucopolysaccharides (page 758 and page 1458).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use various capping molecules in the xenografts with a reasonable expectation of success in making xenograft products suitable for transplantation because various capping molecules including glucosamine and sialic acid are widely distributed in mucoproteins and mucopolysaccharides of animal tissues and, thus, they considered to be biochemically functional equivalents. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

The applied references US 6,110,206 [IDS-A37], US 5,944,755 [IDS-A33], US 5,782,915 [IDS-A28] and US 5,922,027 [IDS-A32] have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, they constitute prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference

was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova, Art Unit 1651

September 5, 2002.

IRENE MARX
PRIMARY EXAMINER